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FELFE & LYNCH

By

ROGO 211.2-NDH

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s)	:	Thomas S. Parker, et al.
Serial No.	:	08/487,461
Filed	:	June 7, 1995
For	:	METHODS AND COMPOSITIONS USEFUL IN PROPHYLAXIS AND THERAPY OF ENDOTOXIN RELATED CONDITIONS
Group Art Unit	:	
Examiner	:	

September 22, 1995

Hon. Commissioner of Patents
and Trademarks
Washington, D.C. 20231

INFORMATION DISCLOSURE STATEMENT

S I R:

In accordance with their duty of disclosure, applicants wish to make the accompanying references of record in the above identified application:

Schwarzenberg, et al, "Ursodeoxycholic Acid Modifies Gut-Derived Endotoxemia In Neonatal Rats", Ped. Res. 35(2):214-217 (1994)

shows the use of "UCDA" in a rat model, with clearance of endotoxin (LPS).

Calmus, et al, "Differential Effects of Chenodeoxycholic and Ursodeoxycholic Acids on Interleukin 1, Interleukin 6 and Tumor Necrosis Factor-α Production by Monocytes", Hepatology 16(3):719-723 (1992), shows how the above referenced materials inhibited the production of IL-1, IL-6, and TNFα, and hence might be considered an immunosuppressive agent.

Pain, et al, "Prevention of Postoperative renal dysfunction in patients with obstructive jaundice: a multicentre study of bile salts and lactulose", Br. J. Surg. 78:467-469 (1991) described how the administration of bile salts, orally, helped to inhibit systemic endotoxemia in renal failure patients.

Greve, et al, "Bile Acids Inhibit Endotoxin - Induced Release of Tumor Necrosis Factor By Monocytes: An In Vitro Study", Hepatology 10(4);454-458 (1989) discuss results which contraindicate the use of bile acids to inactivate endotoxins. Note page 457, first column, end through line 4 of this second column.

Cahill, et al, "Bile Salts, Endotoxin And Renal Function In Obstructive Jaundice", Surg. Gynec. & Obstet. 165:519-522 (12/87) discuss how chenodeoxycholic acid reduced endotoxemia but not significantly, and did not help restore renal function in a patient population.

Thompson, et al, "A randomized clinical trial of oral ursodeoxycholic acid in obstructive jaundice", Br. J. Surg. 73:634:636 (1986) describe a reduction in portal endotoxemia when ursodeoxycholic acid was used.

Hoffmann, "Chemistry and Enterohepatic Circulation of Bile Acids", Hepatology 4(5):4S-14S (1984) provides an extensive listing of various bile acids. Note, e.g., table 1 at page 75.

Bertok, "Physico-Chemical Defense of Vertebrate Organisms: The Role of Bile Acids In Defense Against Bacterial Endotoxins", Persp. Biol and Med. 1977:70-75 (Autumn 1977) discuss, at page 72, resistance to orally administered endotoxin following treatment with sodium deoxycholate.

Kocsar, et al, "Effect of Bile Acids on the Intestinal Absorption of Endotoxin In Rats", J. Bacteriol 100(1):220-223 (1969), shows

that, in a rat model, endotoxin from the peritonial cavity was reduced following adminstration of sodium deoxycholate.

Ribi, "Reaction of Endotoxin and Surfactants", J. Bacteriol 92(5):1493-1509 (1966) teach that various surfactants react with endotoxins.

It is submitted that the claimed subject matter is patentable over this art, and a holding to that end is urged.

Respectfully submitted,

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